ORC4 gene

origin recognition complex subunit 4

Normal Function

The *ORC4* gene provides instructions for making a protein that is important in the copying of a cell's DNA before the cell divides (a process known as DNA replication). The protein produced from this gene, ORC4, is one of a group of proteins known as the origin recognition complex (ORC). (The complex is made up of the proteins ORC1 to ORC6, which are produced from different genes.) ORC attaches (binds) to certain regions of DNA known as origins of replication (or origins), where the process of DNA copying begins. This complex attracts additional proteins to bind to it, forming a larger group of proteins called the pre-replication complex. When the pre-replication complex is attached to the origin, replication is able to begin at that location. This tightly controlled process, called replication licensing, helps ensure that DNA replication occurs only once per cell division and is required for cells to divide.

ORC also attaches to a form of DNA called heterochromatin. Heterochromatin is densely packed DNA that contains few functional genes, but it is important for controlling gene activity and maintaining the structure of chromosomes. It is unclear what effect ORC binding has on heterochromatin.

Health Conditions Related to Genetic Changes

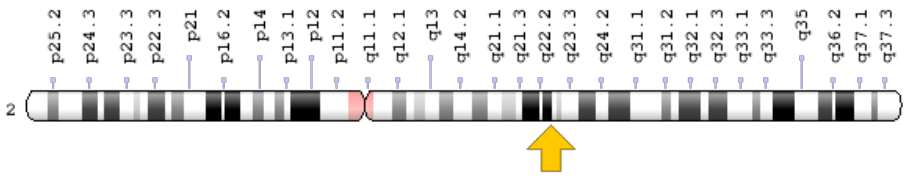
Meier-Gorlin syndrome

Mutations in the *ORC4* gene cause Meier-Gorlin syndrome, a condition characterized by short stature, underdeveloped kneecaps, and small ears. These mutations alter the ORC4 protein, typically by changing single protein building blocks (amino acids) or by leading to production of an abnormally short version of the ORC4 protein. The most common *ORC4* gene mutation in people with this condition replaces the amino acid tyrosine at position 174 with the amino acid cysteine (written as Tyr174Cys). As a result of these changes, assembly of the pre-replication complex is impaired, which disrupts replication licensing; however, it is not clear how a reduction in replication licensing leads to Meier-Gorlin syndrome. Researchers speculate that such a reduction delays the cell division process, which slows growth of the bones and other tissues during development. It is not known why development of the kneecaps and ears is particularly affected.

Chromosomal Location

Cytogenetic Location: 2q23.1, which is the long (q) arm of chromosome 2 at position 23.1

Molecular Location: base pairs 147,930,397 to 148,021,604 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HsORC4
- ORC4_HUMAN
- ORC4L
- ORC4P
- origin recognition complex, subunit 4
- origin recognition complex, subunit 4 homolog

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): DNA Synthesis Begins at Replication Origins
  https://www.ncbi.nlm.nih.gov/books/NBK26826/#_A796_
- The Cell: A Molecular Approach (second edition, 2000): Origins and the Initiation of Replication
  https://www.ncbi.nlm.nih.gov/books/NBK9940/#_A789_

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ORC4%5BTIAB%5D%29+OR+%28%28HsORC4%5BTIAB%5D%29+OR+%28ORC4L%5BTIAB%5D%29+OR+%28ORC4P%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- ORIGIN RECOGNITION COMPLEX, SUBUNIT 4, S. CEREVISIAE, HOMOLOG OF
  http://omim.org/entry/603056

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ORC4.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ORC4%5Bgene%5D
- HGNC Gene Family: AAA ATPases
  http://www.genenames.org/cgi-bin/genefamilies/set/413
- HGNC Gene Family: Origin recognition complex
  http://www.genenames.org/cgi-bin/genefamilies/set/960
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=8490
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5000
- UniProt
  http://www.uniprot.org/uniprot/O43929

Sources for This Summary

- Bicknell LS, Bongers EM, Leitch A, Brown S, Schoots J, Harley ME, Aftimos S, Al-Aama JY, Bober M, Brown PA, van Bokhoven H, Dean J, Edrees AY, Feingold M, Fryer A, Hoefsloot LH, Kau N, Knoers NV, Mackenzie J, Opitz JM, Sarda P, Ross A, Temple IK, Toutain A, Wise CA, Wright M, Jackson AP. Mutations in the pre-replication complex cause Meier-Gorlin syndrome. Nat Genet. 2011 Feb 27;43(4):356-9. doi: 10.1038/ng.775.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21358632
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3068194/
- Guernsey DL, Matsuoka M, Jiang H, Evans S, Macgillivray C, Nightingale M, Perry S, Ferguson M, LeBlanc M, Paquette J, Patry L, Rideout AL, Thomas A, Orr A, McMaster CR, Michaud JL, Deal C, Langlois S, Superneau DW, Parkash S, Ludman M, Skidmore DL, Samuels ME. Mutations in origin recognition complex gene ORC4 cause Meier-Gorlin syndrome. Nat Genet. 2011 Feb 27;43(4): 360-4. doi: 10.1038/ng.777.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21358631
- Niida H, Kitagawa M. Regulation of DNA replication licensing. Curr Drug Targets. 2012 Dec;13(13): 1588-92. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22998185
- OMIM: ORIGIN RECOGNITION COMPLEX, SUBUNIT 4, S. CEREVISIAE, HOMOLOG OF http://omim.org/entry/603056
- Prasanth SG, Shen Z, Prasanth KV, Stillman B. Human origin recognition complex is essential for HP1 binding to chromatin and heterochromatin organization. Proc Natl Acad Sci U S A. 2010 Aug 24;107(34):15093-8. doi: 10.1073/pnas.1009945107. Epub 2010 Aug 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20689044
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2930523/

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